REMARKS

Claims 24, 26, and 28-32 are currently pending in the application. Claim 32 is amended. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

Rejection of Claim 32 Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claim 32 under § 112, second paragraph as being allegedly indefinite in the use of the phrase "as evidenced by an *in vitro* assay". The Office Action asserts that it is unclear what is meant by the terms "evidenced" or "assays". Applicants respectfully disagree.

Claim 32 has been amended to delete the phrase "as evidenced by an *in vitro* assay", and is now in the same form as originally presented. Claim 32 has been previously rejected as indefinite for failing to create the essential steps for "detecting a Th1 immune response". After further consideration, Applicants believe that Claim 32 is definite as originally written. Amended claim 32 recites further limitations on the step of "assaying" recited in claim 24 by requiring that "assaying" comprises the steps of "administering" and "detecting". While Applicants acknowledge the requirement, as set out in MPEP §2172.01, that claims recite essential elements, the function of 35 U.S.C. §112, second paragraph, and thus the focus of an analysis of whether a claim complies with the statue, is to ensure that the claims apprise one of skill in the art of their scope and, therefore, serve the notice function required by the statute; by providing clear warning to others as to what constitutes infringement. See, e.g., *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379 (Fed. Cir. 2000); MPEP, §2173.02. The case law is clear that a decision on whether a claim is invalid under § 112, second paragraph, requires a determination of **whether those skilled in the art would understand what is claimed when the claim is read in light of the specification**. *Seattle Box Co. v. Industrial Crating & Packing Inc.*, 731 F.2d 818, 826, 221 U.S.P.Q. (BNA) 568, 574 (Fed. Cir. 1984); *In re Marosi*, 710 F.2d 799, 803, 218 U.S.P.Q. (BNA) 289, 292 (Fed. Cir. 1983). Applicants are only required to claim the invention with a **reasonable** degree of particularity and distinctness; satisfaction of §112,

second paragraph is to be judged using a reasonableness standard. MPEP, §2173.02. **It is not the function of the claims to serve as a laboratory manual.**

Claim 32 recites the step of "detecting a Th1 immune response". The specification teaches on pages 21 to 24, and 30-34, methods for detecting a Thl immune response in a mammal, using either *in vivo* or *in vitro* assays. Given the language used in claim 32, and the teachings in the specification, one of skill in the art would understood what is being claimed, and would, thus, understand whether they were practicing the claimed invention. To require Applicants to recite specific technical steps for accomplishing detection of a Th1 response, when such steps are clearly set out in the specification, is would force Applicants to unnecessarily narrow the claimed invention. Claim 32 is definite as written, and provides clear warning to others as to what constitutes infringement. Applicants accordingly request that the rejection be reconsidered and withdrawn.

Rejection of Claims 24, 26, and 28-32 Under 35 U.S.C. §103(a)

The Office Action rejected claims 24, 26, and 28-32 under 35 U.S.C. §103 as being unpatentable over Kullberg et al. (J. Immunology, 1992, 148:3264). The Office Action asserts that Kullberg et al tech that the helminthic parasite *Schistosoma mansoni* down regulates the Th1 cytokine secretion of IL-2 and IFN-γ in mice, and that Th1 responses were determined by cytokine profiles as measured by *in vitro* ELISA assays. The Office Action states that Kullberg et al. differ from the claimed invention in that they do not teach steps of fractionating, sub-fractionating and testing of the sub-fractions. The Office Action asserts that, since methods of fractionation and sub-fractionation are well known and routine, one of skill in the art would have been motivated to use such methods to identify the component of the parasite composition responsible for downregulation of Th1 cytokine secretion as taught by Kullberg et al. The Office Action asserts that one of skill in the art would have been motivated to identify the components in order to produce a "pure" composition capable of reducing a Th1 response without possible negative effects caused by the other constituents of the nematode composition. Applicants respectfully disagree.

One of skill in the art, given the teachings in Kullberg et al., would not have been motivated to make fractions and subfractions of the *S. mansoni* preparations taught therein to produce a pure composition capable of reducing a Th1 response. Kullberg et al. report on cytokine production in spleen cells obtained from *S. mansoni* infected mice, following stimulation with a non-parasite antigen (sperm whale myoglobin; SwMb). Kullberg et al. report that Th1 immune responses to SwMb are decreased in *S. mansoni* infected mice compared to un-infected mice. Kullberg et al. focus only on the implications of *S. mansoni* infection on the response of the infected mammal to non-parasite antigen. For example, Kullberg et al. teach that "the results presented here may have implications for intercurrent infection...[i]nfected individuals may have an increased susceptibility to infections normally cleared by Th1-dependent immunity as well as altered immune response after vaccinations" (p. 3269, col. 2, last paragraph). In addition, Kullberg et al. refer to the infected mice merely as a "murine *S. mansoni* model", useful to determine immune response to non-parasite antigen (p. 3269, col. 2., last paragraph). There is no teaching or suggestion in Kullberg et al. that *S. mansoni* preparations could or should be used to decrease Th1 immune responses. Moreover, there is no teaching or suggestion in Kullberg et al. that *S. mansoni* could or should be used as a therapeutic agent. Thus, one of skill in the art, regardless of how routine the technical steps of fractionation and sub-fractionation are, would not have been motivated to endeavor to identify an active fraction of *S. mansoni* because there is no teaching in Kullberg et al. relating to the use of *S. mansoni* with the goal of reducing a Th1 response. The pending claims are therefore non-obvious over the teachings of Kullberg et al. and Applicants request that the rejection be reconsidered and withdrawn.

The Office Action also rejected claims 24, 26, and 28-32 as unpatentable over Lee et al. (WO 96/29802). The Office Action asserts that Lee et al. teach the down regulation of Th1 activity in mice can be accomplished by administration of a soluble helminthic nematode extract. The Office Action states that Lee et al. do not teach the steps of fractionation, sub-fractionation, and sub-fraction testing. The Office Action asserts that, since methods of fractionation and sub-fractionation are well known and routine, one of skill in the art would have been motivated to use such methods to identify the component of the parasite composition responsible for downregulation of Th1 cytokine secretion as taught by Lee et al. The Office Action asserts that

one of skill in the art would have been motivated to identify the components in order to produce a "pure" composition capable of reducing a Th1 response without possible negative effects caused by the other constituents of the nematode composition. Applicants respectfully disagree.

One of skill in the art, given the teachings of Lee et al., would not have been motivated to perform the steps of fractionation, sub-fractionation, and testing of the sub-fractions to identify an active component of the helminthic preparation because there is no teaching or suggestion in Lee et al. to identify an active component. It is well settled law that even when a finding of obviousness is based on a single prior art reference, there must be a showing of a suggestion or motivation to modify the teachings of that reference. See, *B.F. Goodrich Co. v. Aircraft Breaking Sys. Corp.*, 72 F.3d 1577, 1582 (Fed. Cir. 1997). In addition, the showing of motivation must be clear and particular; broad conclusory statements about the teaching are not evidence of motivation. See, *In re Dembiczak*, 175 F.3d 994, 1000 (Fed. Cir. 1999). There is no teaching or even a suggestion by Lee et al. to fractionate a helminthic preparation, assaying a fraction to determine whether the fraction decreases a Th1 immune response, further fractionate the initial fraction, and then assay the sub-fraction to identify a sub-fraction that reduces a Th1 immune response.

The Office Action relies on the assertion that the technical know-how to fractionate a sample was known in the art, to find the requisite motivation to modify the teachings of Lee et al. beyond what is taught or suggested in the reference. It is clear law that the mere fact that a device or process utilizes known scientific principle does not alone make that device or process obvious. *Uniroyal, Inc. v. Rudkin-Wiley Corp.*, 837 F.2d 1044 (Fed. Cir. 1988). In this case, the mere fact that fractionation was technically feasible would not have motivated one of skill in the art to modify the teachings of Lee et al., particularly where Lee et al. report better allograft survival rates using active, live helminth infection. There is simply no teaching or suggestion in Lee et al. that would motivate one of skill in the art to perform the steps required by the instant claims. Claims 24, 26, and 28-32 are, therefore, non-obvious over the teachings of Lee et al., and Applicants request that the rejection be reconsidered and withdrawn.

Applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney/agent of record.

Respectfully submitted,

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